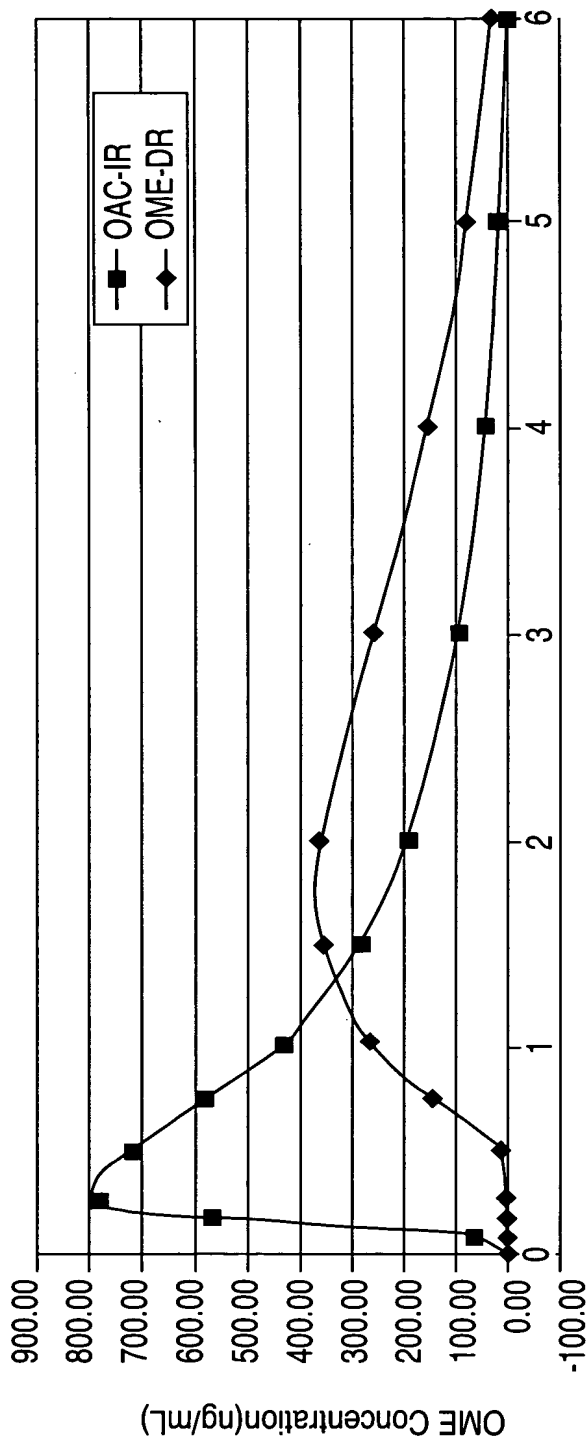




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Pharmacokinetics Of 40mg Omeprazole Formulations  
(Mean Plasma Omeprazole Concentrations From Fasting Subjects\*)

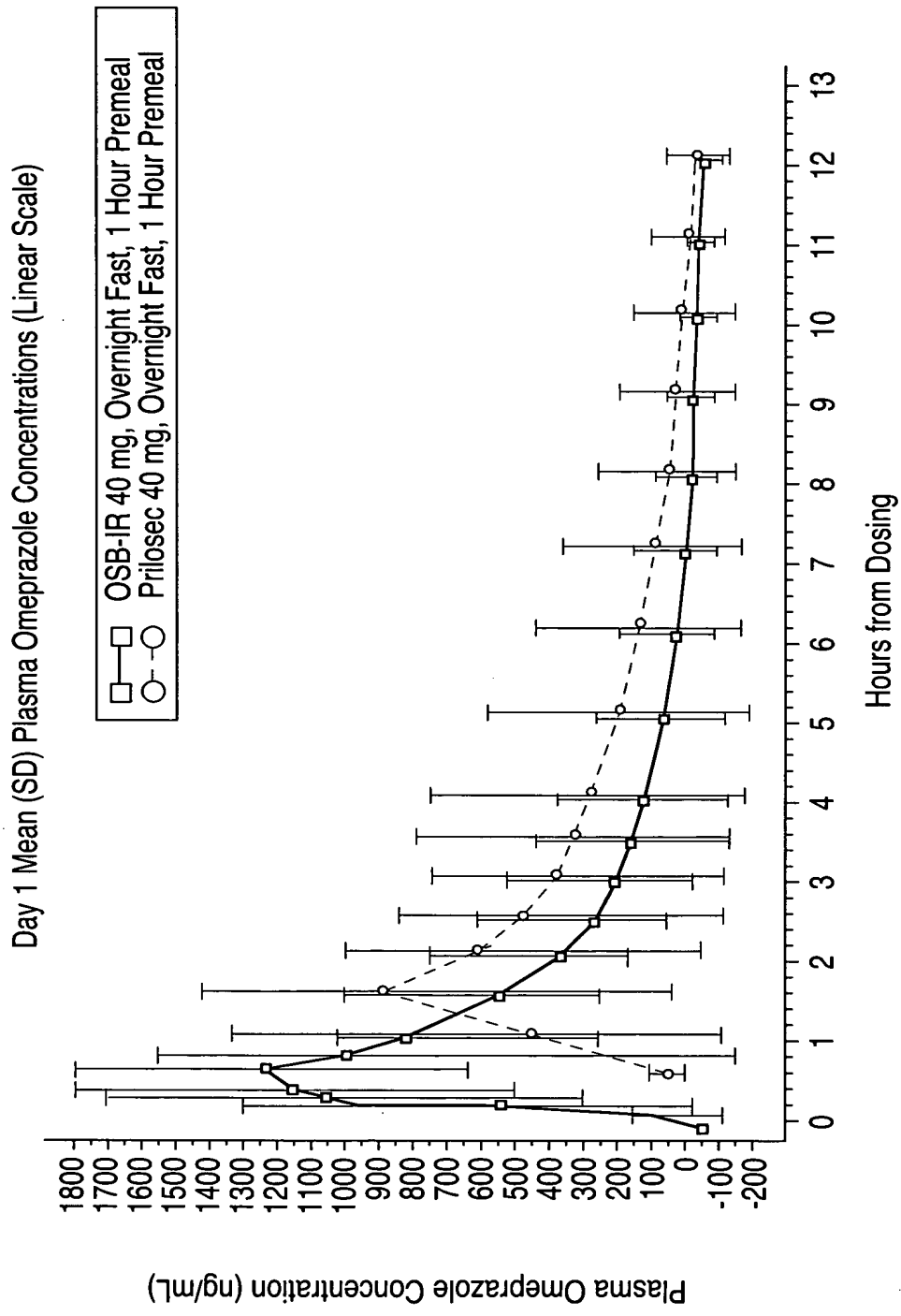


Sampling Times (Hours)

\*for OAC-IR, n=7, for OME-DR, n=10

FIG. 1

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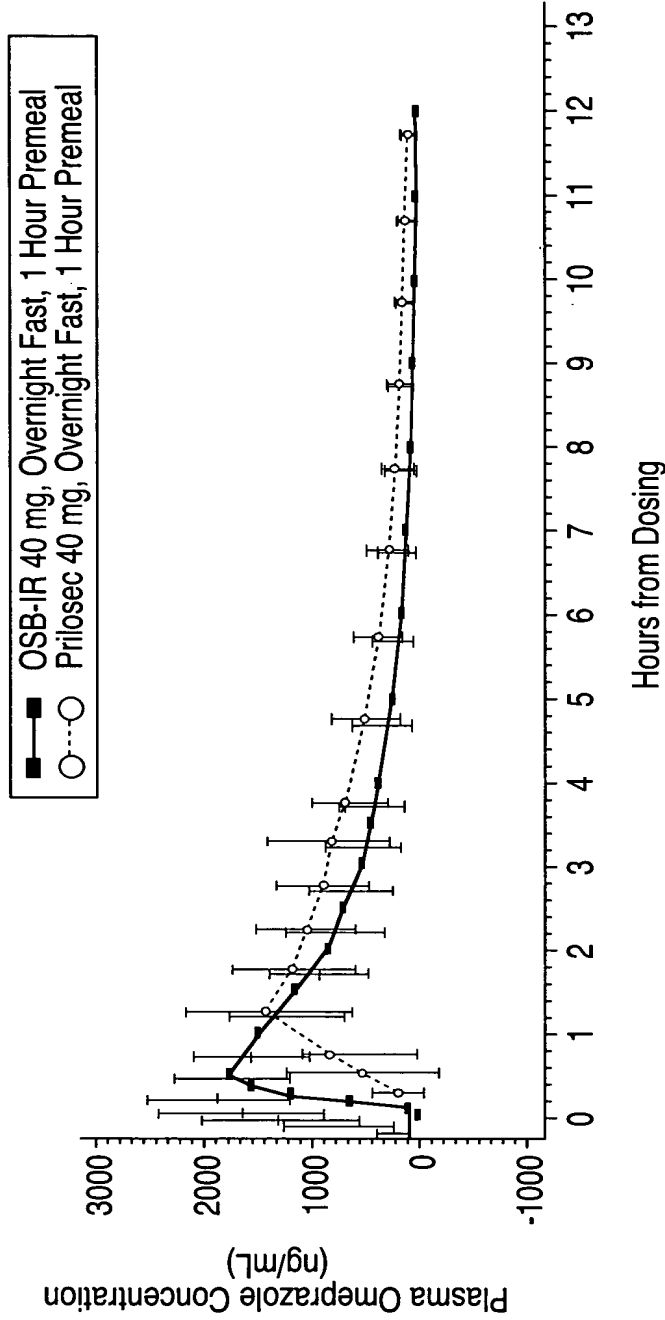


Source: Post-text Tables 15.4-1 and 15.4-4.  
Note: The entire curve for Prilosec 40 mg treatment is shifted slightly (3 minutes) to the right for ease of reading. Both curves were generated from blood samples taken at the identical time points as indicated for the OSB-IR curve.

**FIG. 2**

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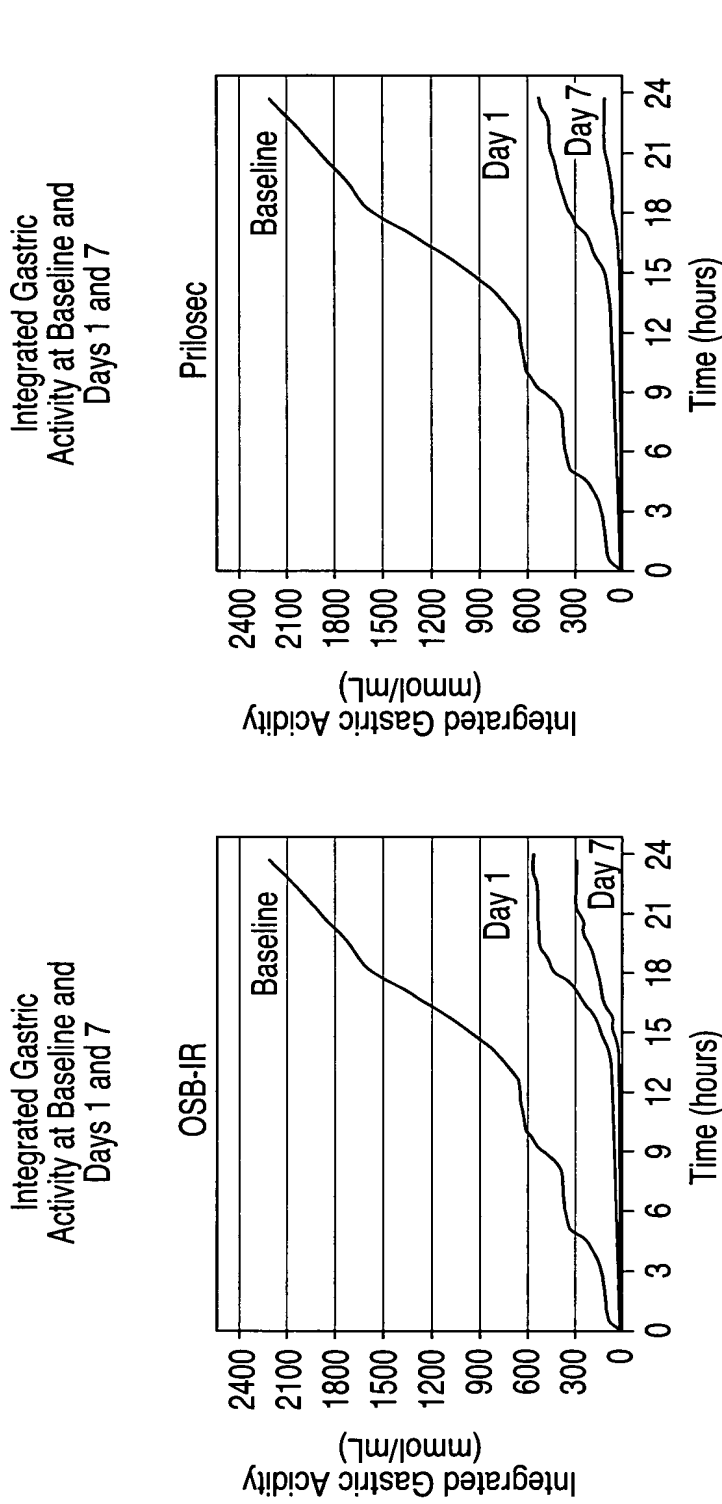
Day 7 Mean (SD) Plasma Omeprazole Concentrations (Linear Scale)



Source: Post-text Tables 15.4-2 and 15.4-5.1.  
Notes: The entire curve for Prilosec 40 mg treatment is shifted slightly (3 minutes) to the right for ease of reading. Both curves were generated from blood samples taken at the identical time points as indicated for the OSB-IR curve.

**FIG. 3**

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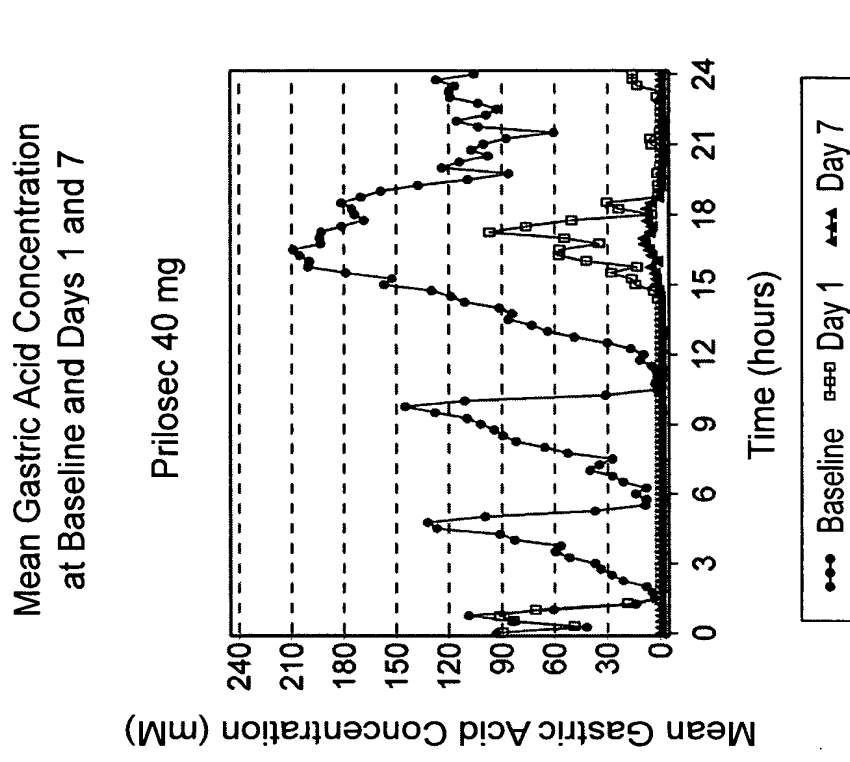
Notes: Zero time is the time of dosing. The time curve was plotted using mean values for the 15-minute time intervals over the 24-hour post-dosing recording period. Baseline values were calculated as means from the two baseline recordings. Results are medians from 24 subjects.

Notes: Zero time is the time of dosing. The time curve was plotted using mean values for the 15-minute time intervals over the 24-hour post-dosing recording period. Baseline values were calculated as means from the two baseline recordings. Results are medians from 24 subjects.

**FIG. 4B**

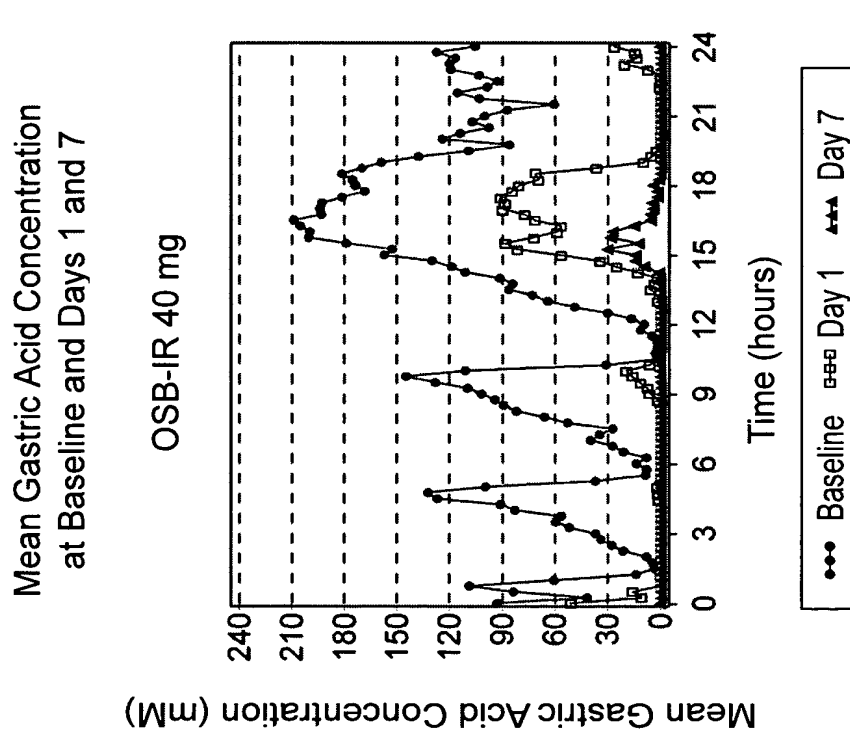
**FIG. 4A**

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**Note:** Zero time is the time of dosing. Values are displayed for each 15-minute interval of the 24-hour post-dosing recording. Baseline values were calculated as means from the two baseline recordings. Results are medians from 24 subjects.

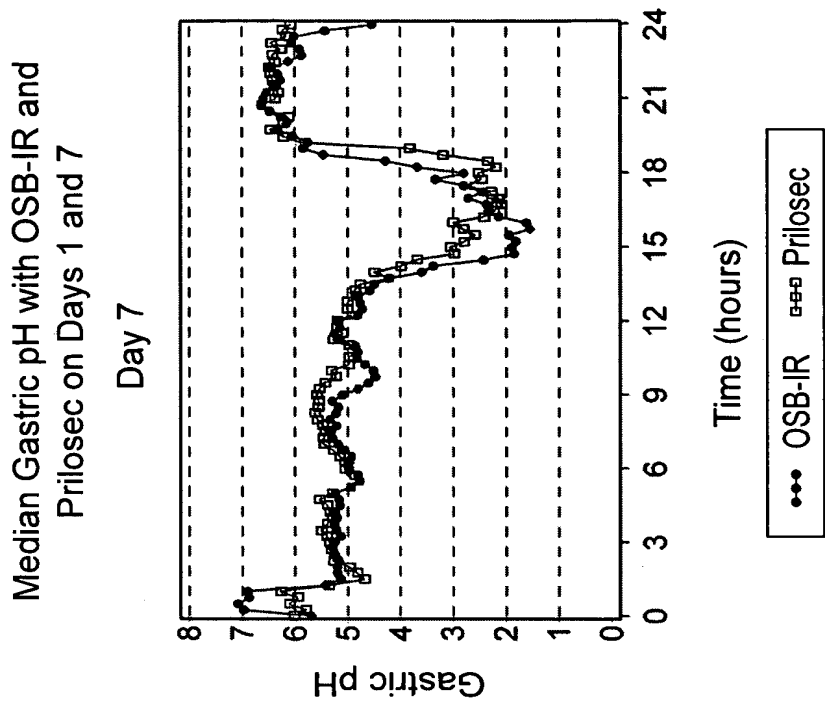
FIG. 5B



**Note:** Zero time is the time of dosing. Values are displayed for each 15-minute interval of the 24-hour post-dosing recording. Baseline values were calculated as means from the two baseline recordings. Results are medians from 24 subjects.

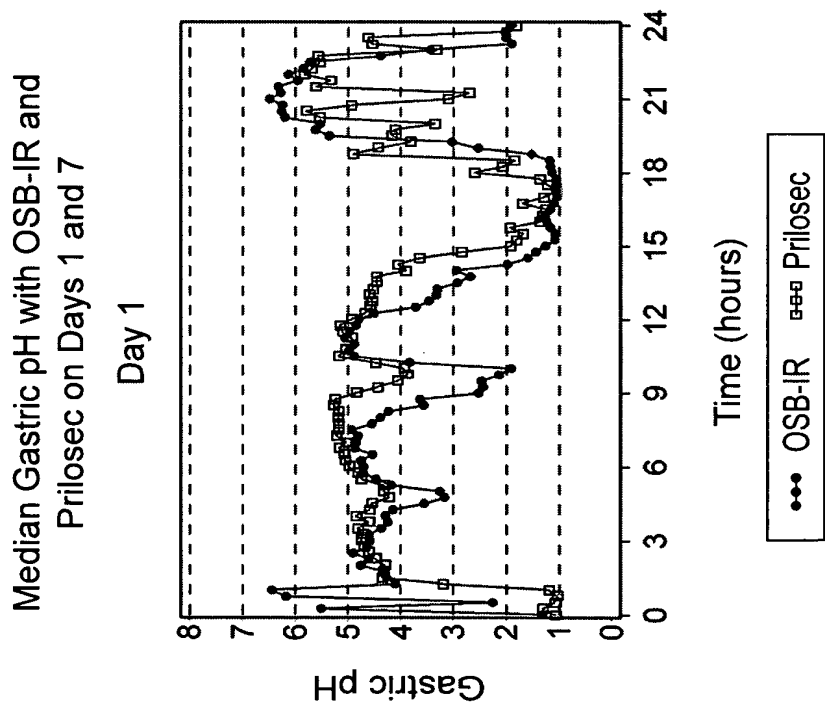
FIG. 5A

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**Note:** Zero time is the time of dosing. Values are displayed for each 15-minute interval of the 24-hour post-dosing recording. Results are medians from 24 subjects.

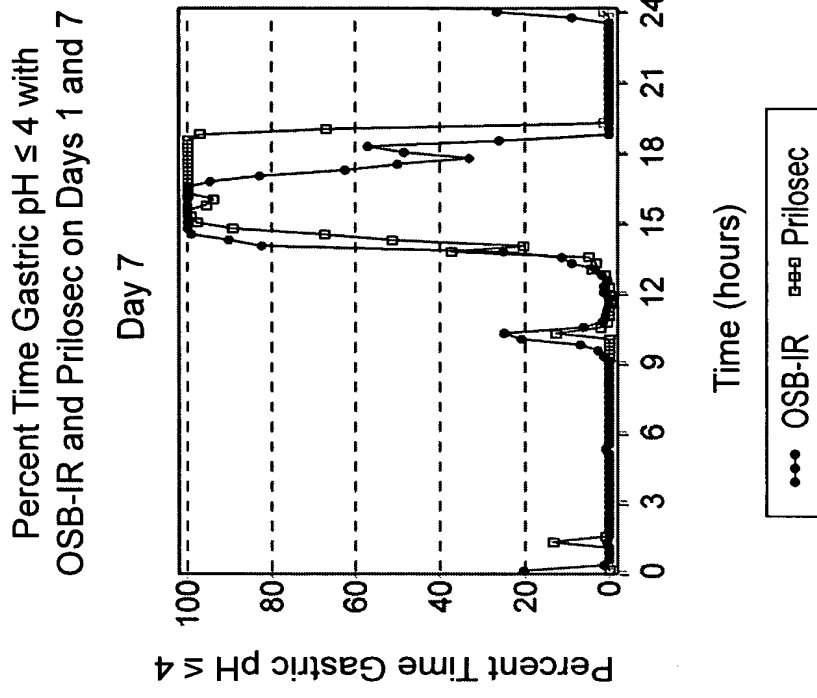
FIG. 6B



**Note:** Zero time is the time of dosing. Values are displayed for each 15-minute interval of the 24-hour post-dosing recording. Results are medians from 24 subjects.

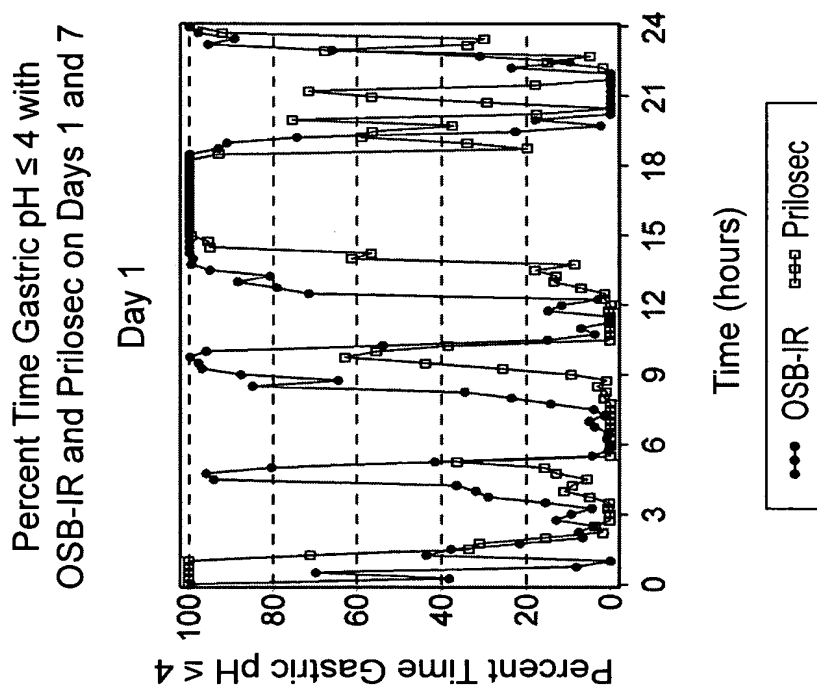
FIG. 6A

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**Note:** Zero time is the time of dosing. Values are displayed for each 15-minute interval of the 24-hour post-dosing recording. Results are medians from 24 subjects.

FIG. 7B



**Note:** Zero time is the time of dosing. Values are displayed for each 15-minute interval of the 24-hour post-dosing recording. Results are medians from 24 subjects.

FIG. 7A

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Comparison of PK/PD Parameters for OSB-IR and Prilosec® 20mg

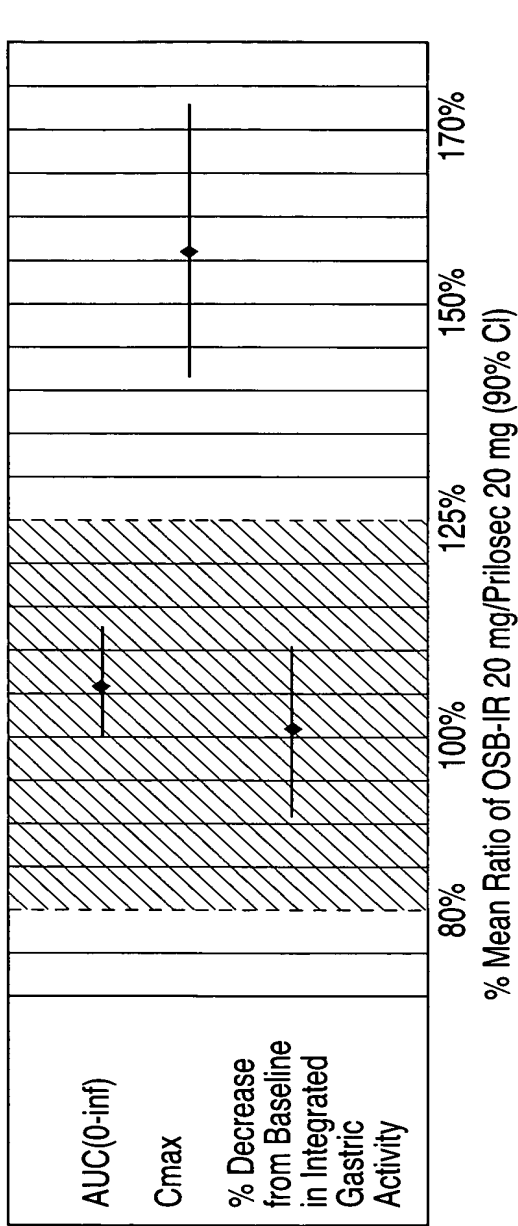


FIG. 8A

Comparison of PK/PD Parameters for OSB-IR and Prilosec® 40mg

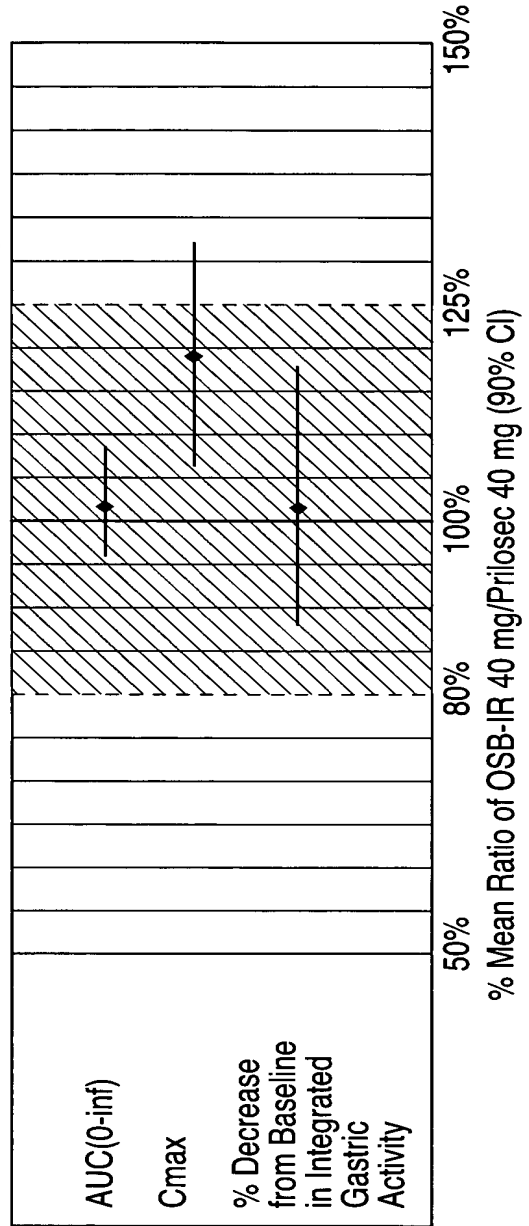
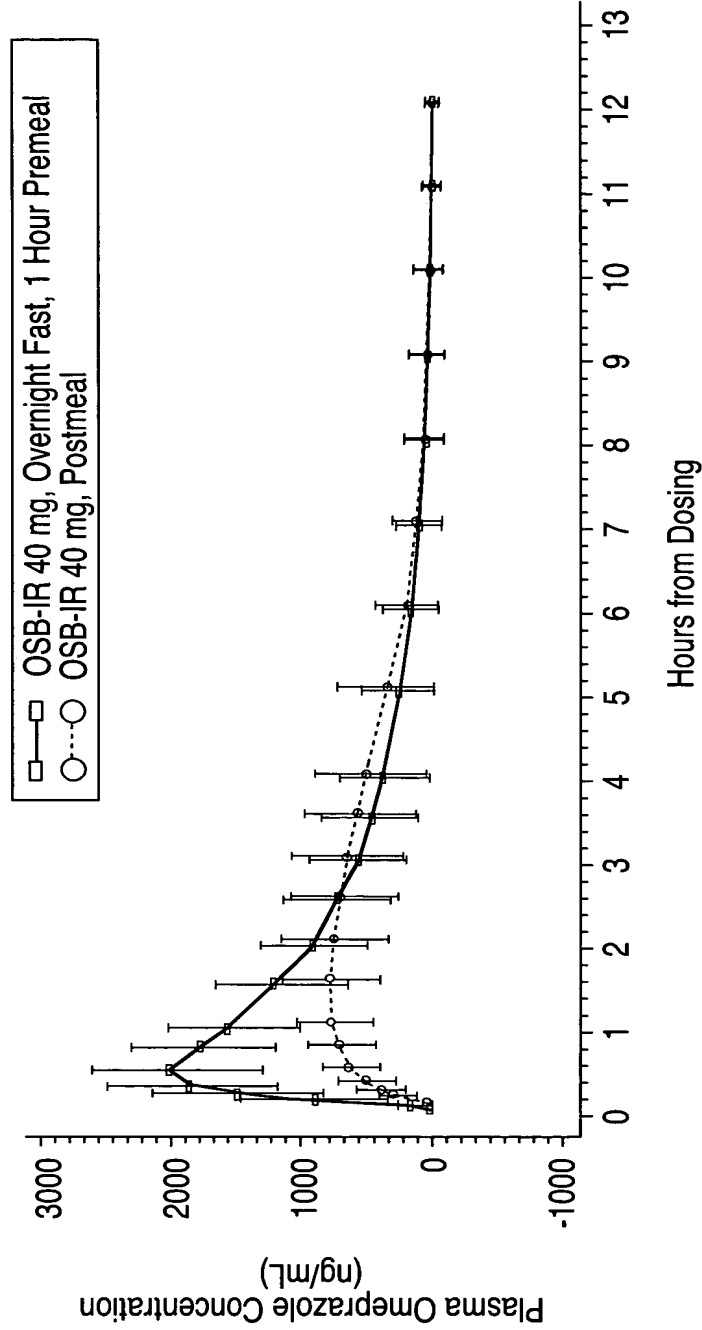


FIG. 8B



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OSB-IR Postmeal (Day 8) vs Premeal (Day 7) Mean (SD) Plasma  
Omeprazole Concentrations at Steady State (Linear Scale)

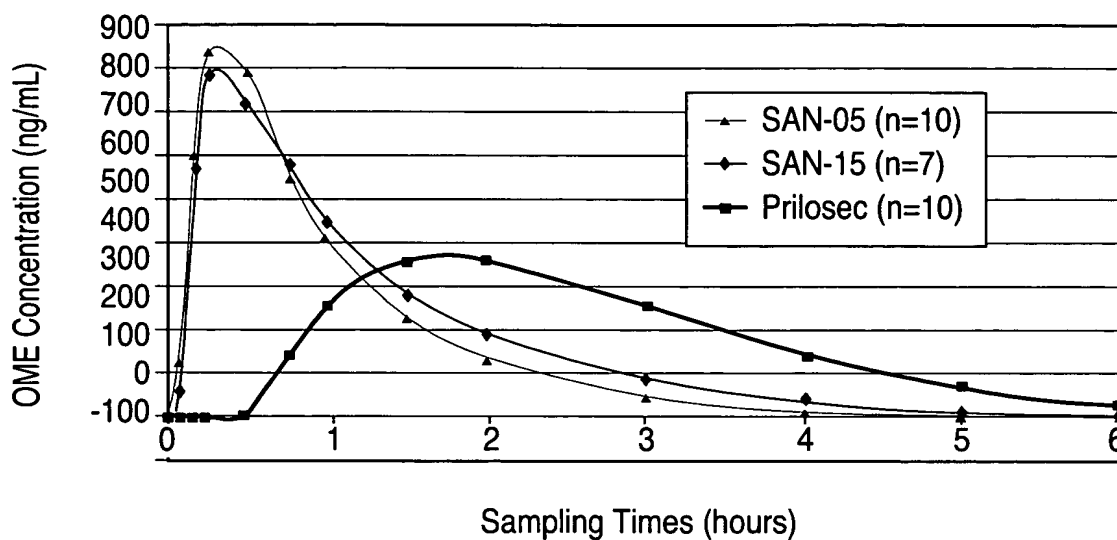


Source: Post-text Tables 15.4-3 and 15.4-15.

Note: The entire curve for OSB-IR 40 mg. Postmeal treatment is shifted slightly (3 minutes) to the right for ease of reading. Both curves were generated from blood samples taken at the identical time points as indicated for the OSB-IR curve.

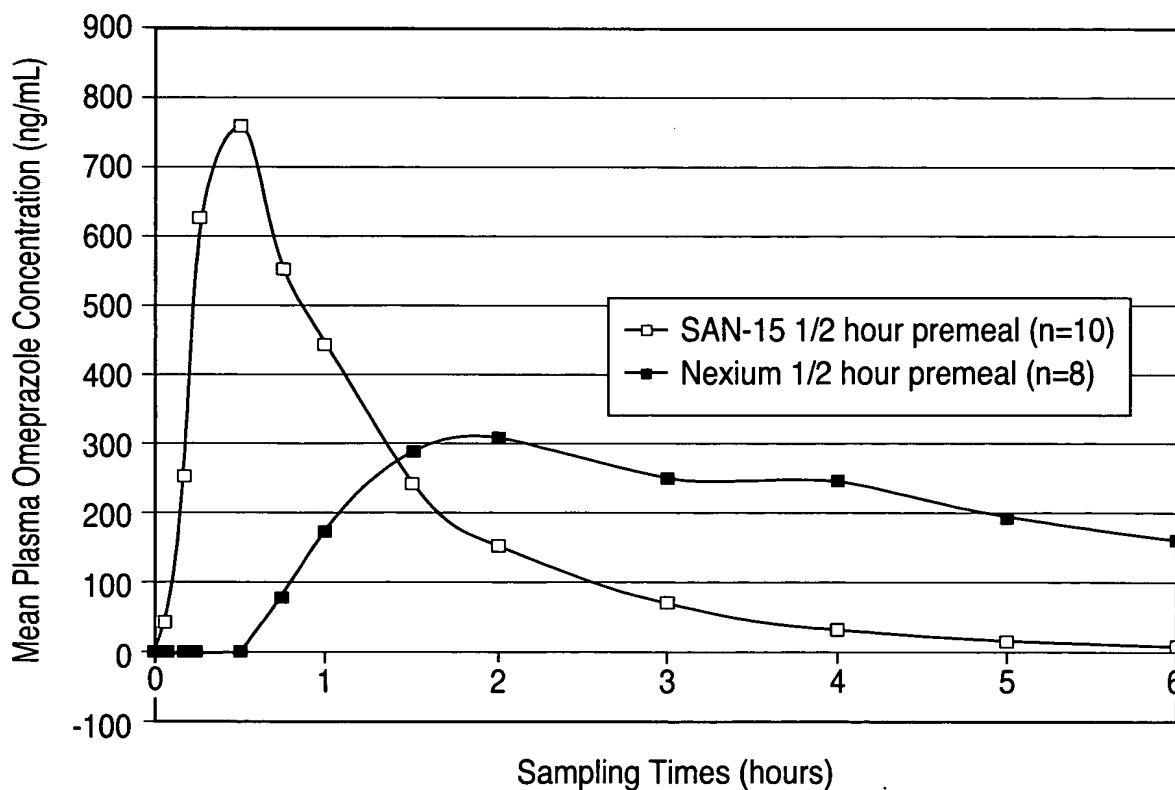
**FIG. 9**

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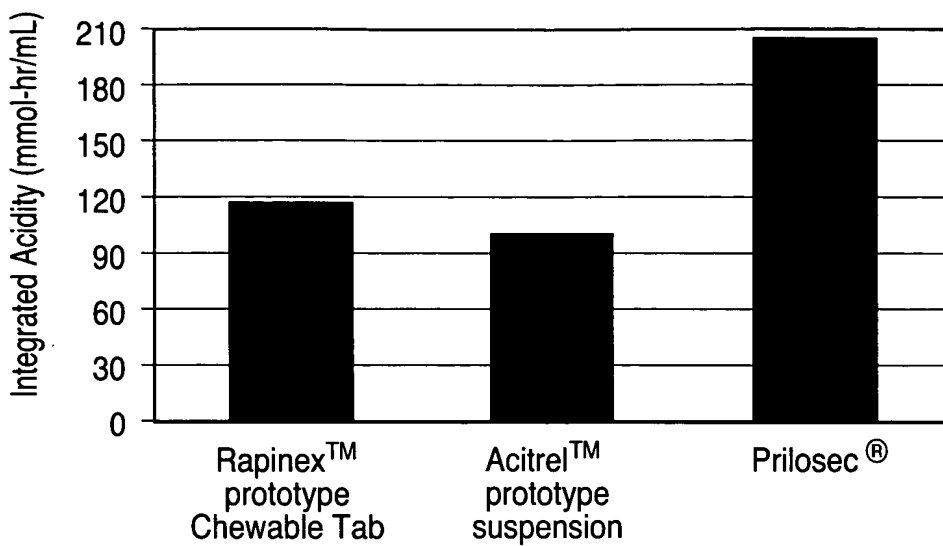
\*mean plasma omeprazole concentrations from fasting subjects

**FIG. 10**



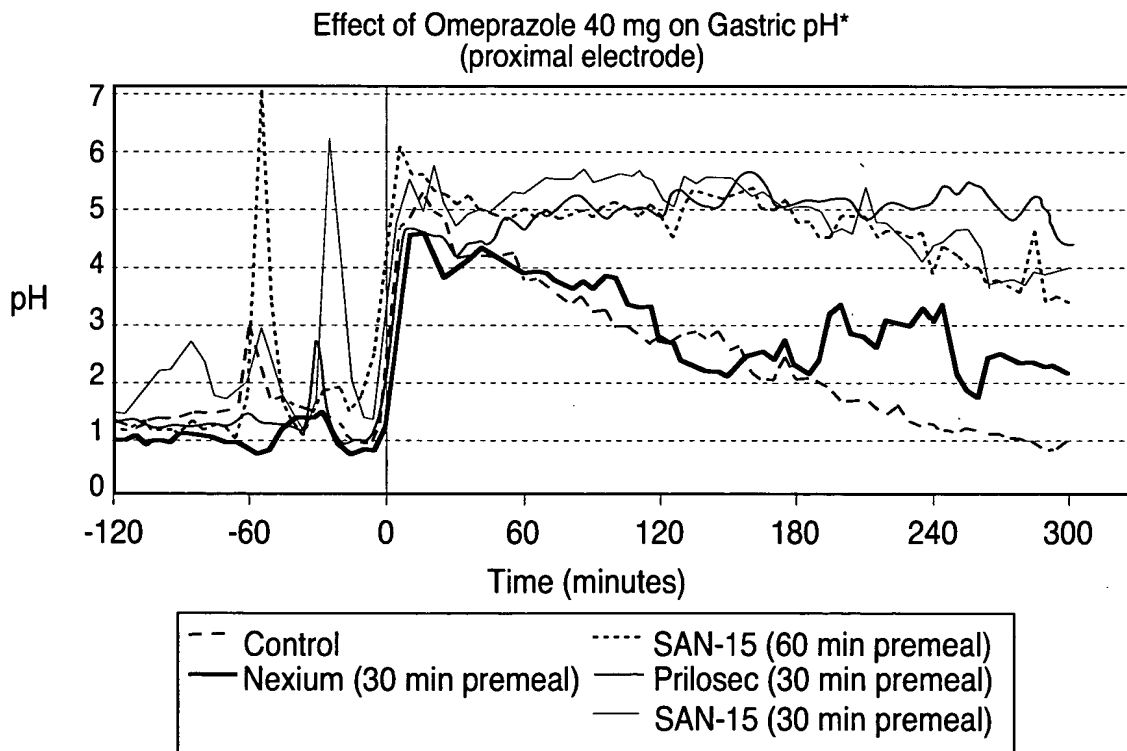
**FIG. 11**

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\*median for all subjects 0-6 h after dosing (40 mg);  
for Rapinex™ prototype, n=7; Acitrel™ prototype, n=10; Prilosec®, n=10

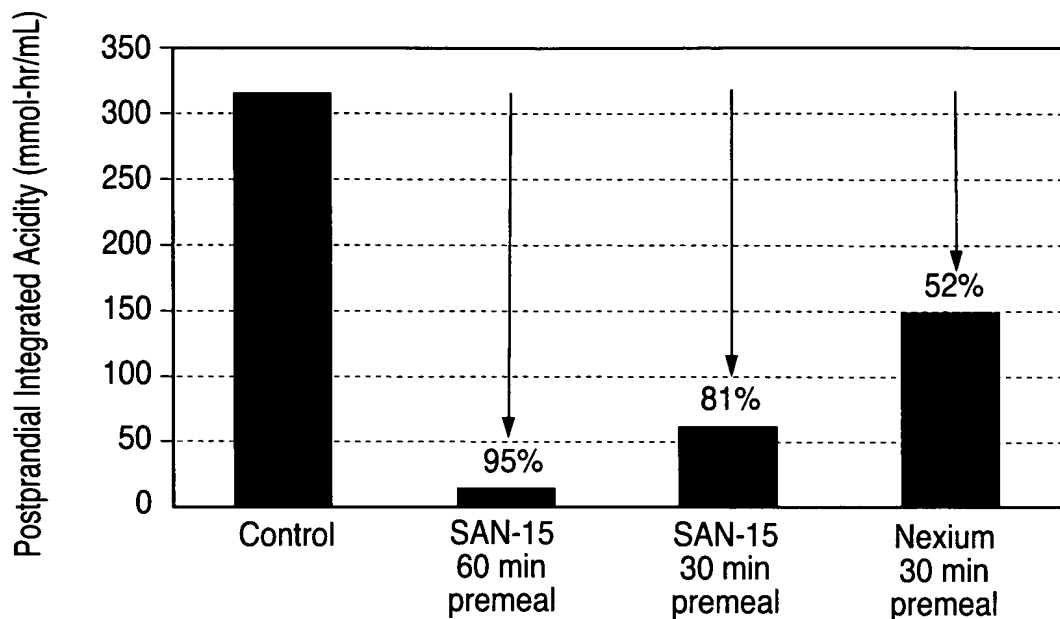
**FIG. 12**



\*median for all subjects; for Control and SAN-15, n=10; for Prilosec and Nexium, n=8

**FIG. 13**

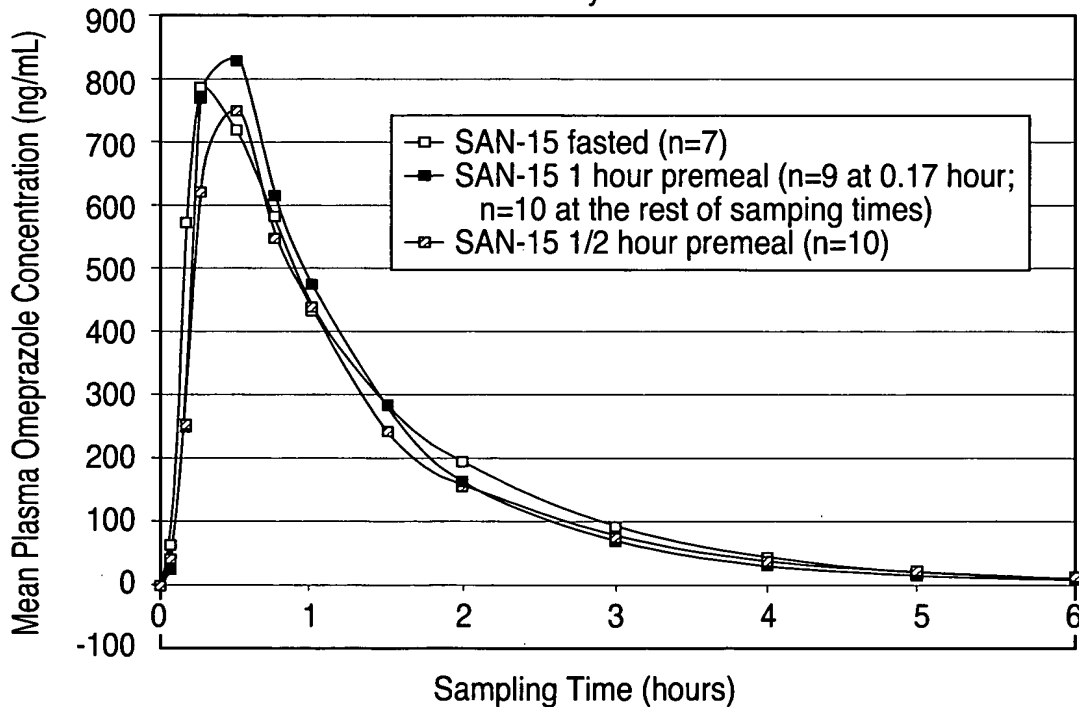
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\*Integrated gastric acidity over 210 minutes; median for all subjects; for Control and SAN-15, n=10 for Nexium®, n=8

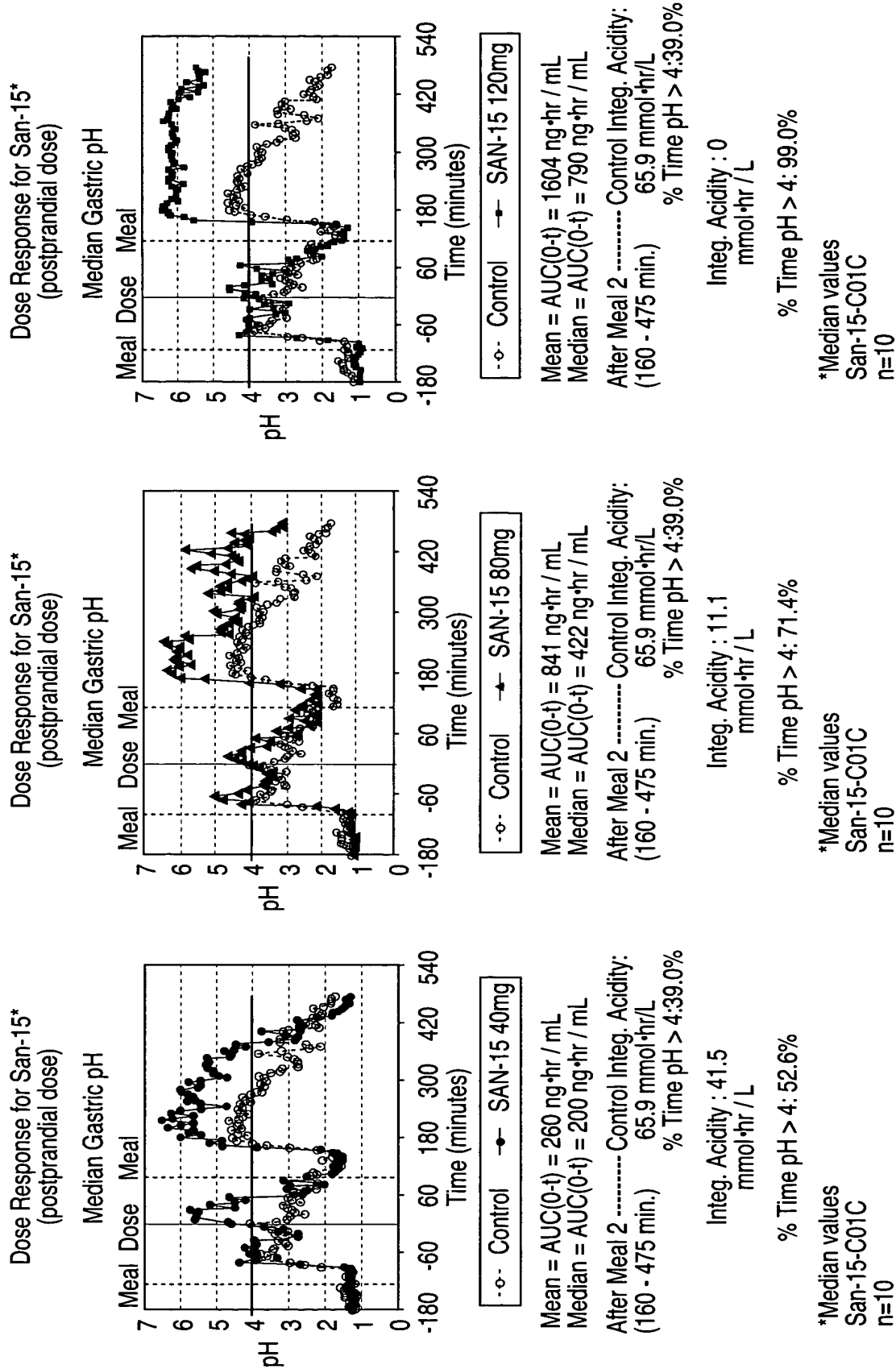
**FIG. 14**

Food Effect (premeal dosing) on  
Bioavailability of SAN-15



**FIG. 16**

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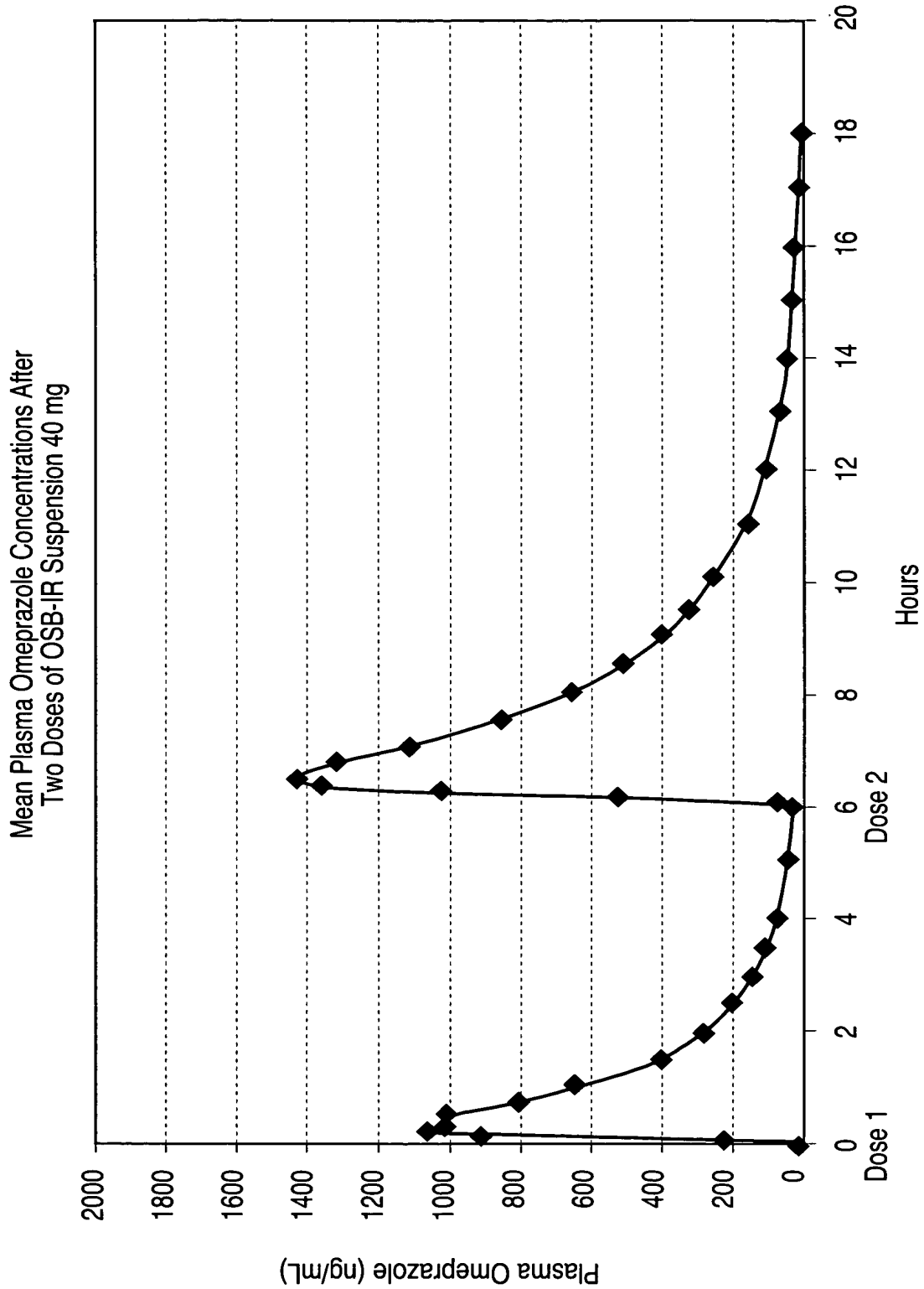


FIG. 17

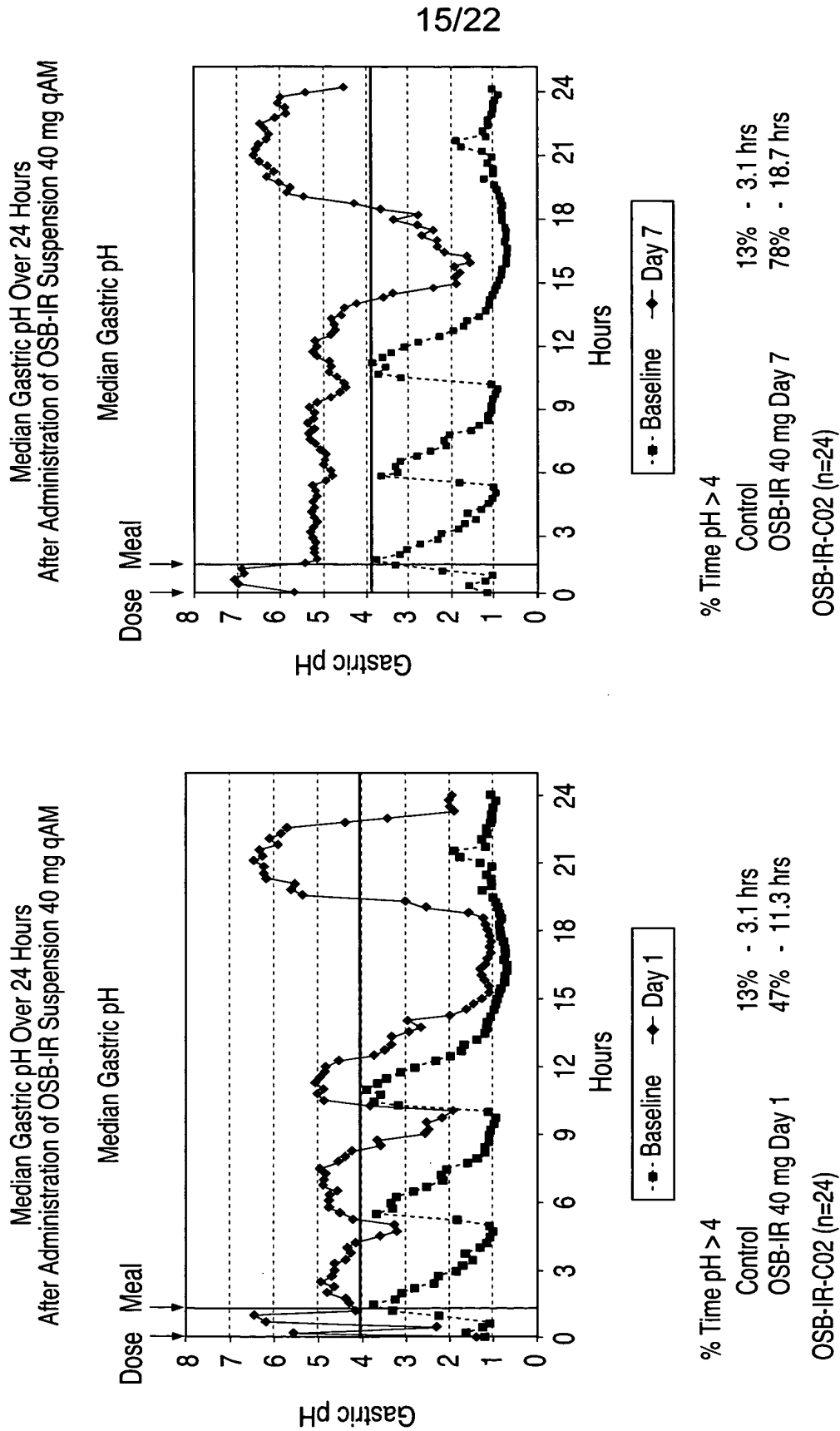
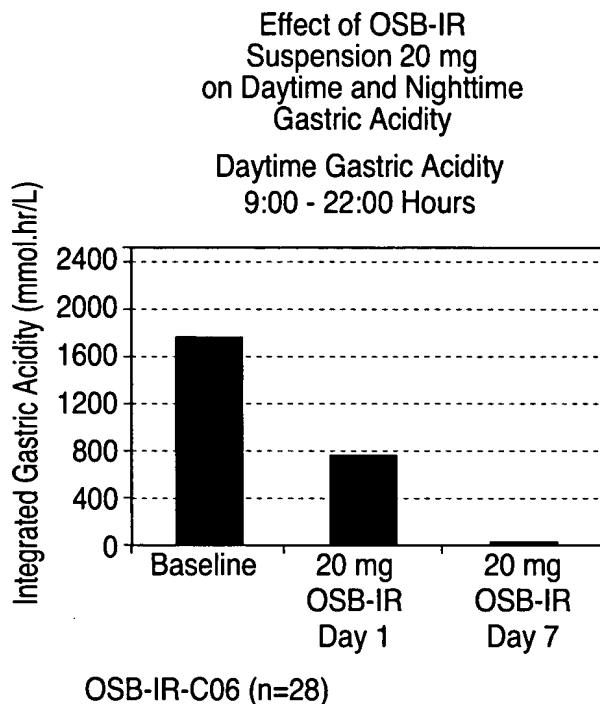


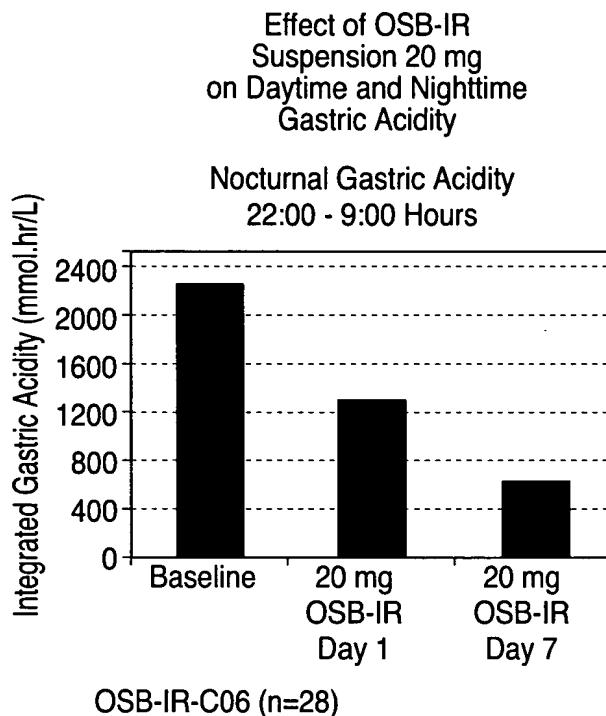
FIG. 18B

FIG. 18A

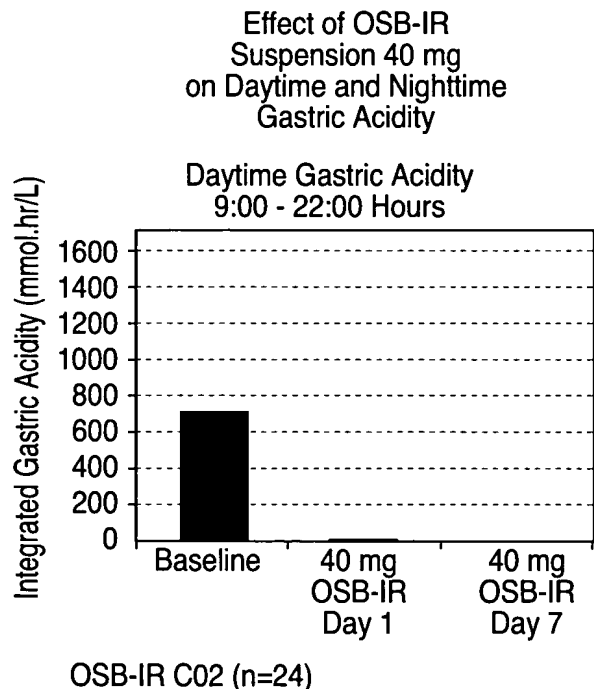
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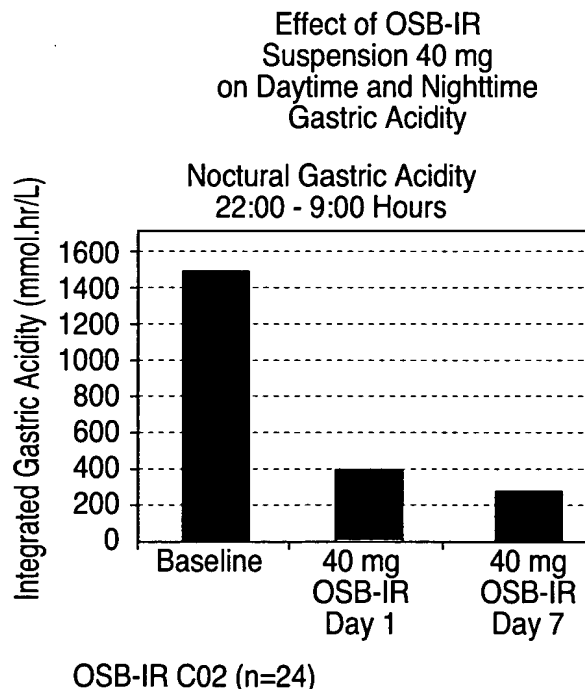
**FIG. 19A**



**FIG. 19B**



**FIG. 20A**

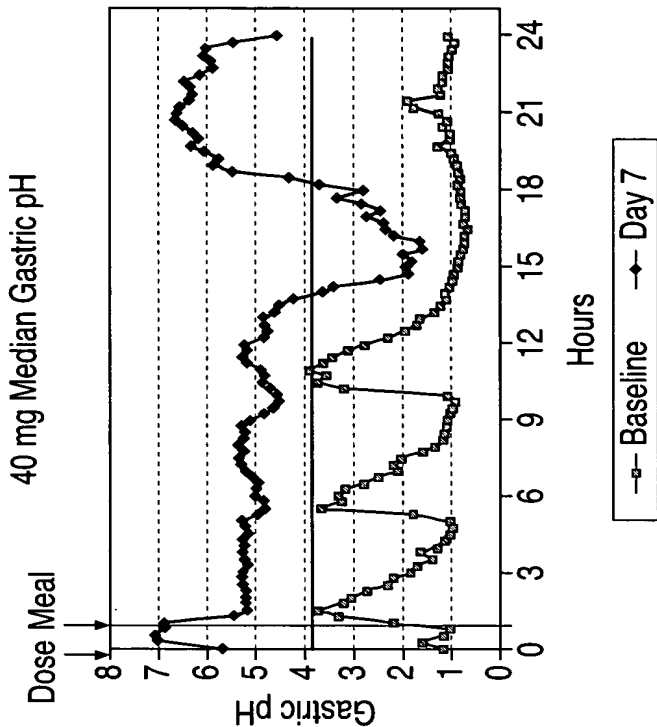


**FIG. 20B**



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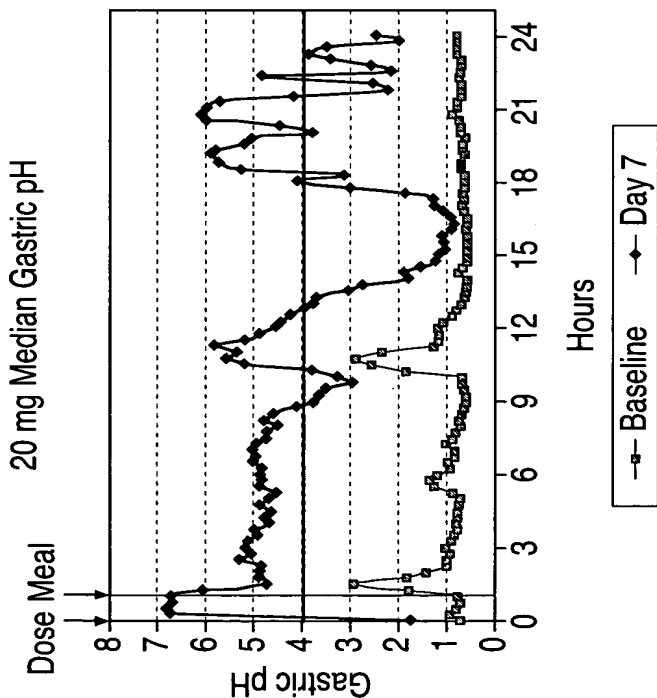
Median Gastric pH Over 24 Hours After Administration  
Of OSB-IR Suspension (Steady State)



% Time pH > 4  
Control 13% - 3.1 hrs  
OSB-IR 40 mg Day 7 78% - 18.7 hrs  
OSB-IR-C02 (n=24)

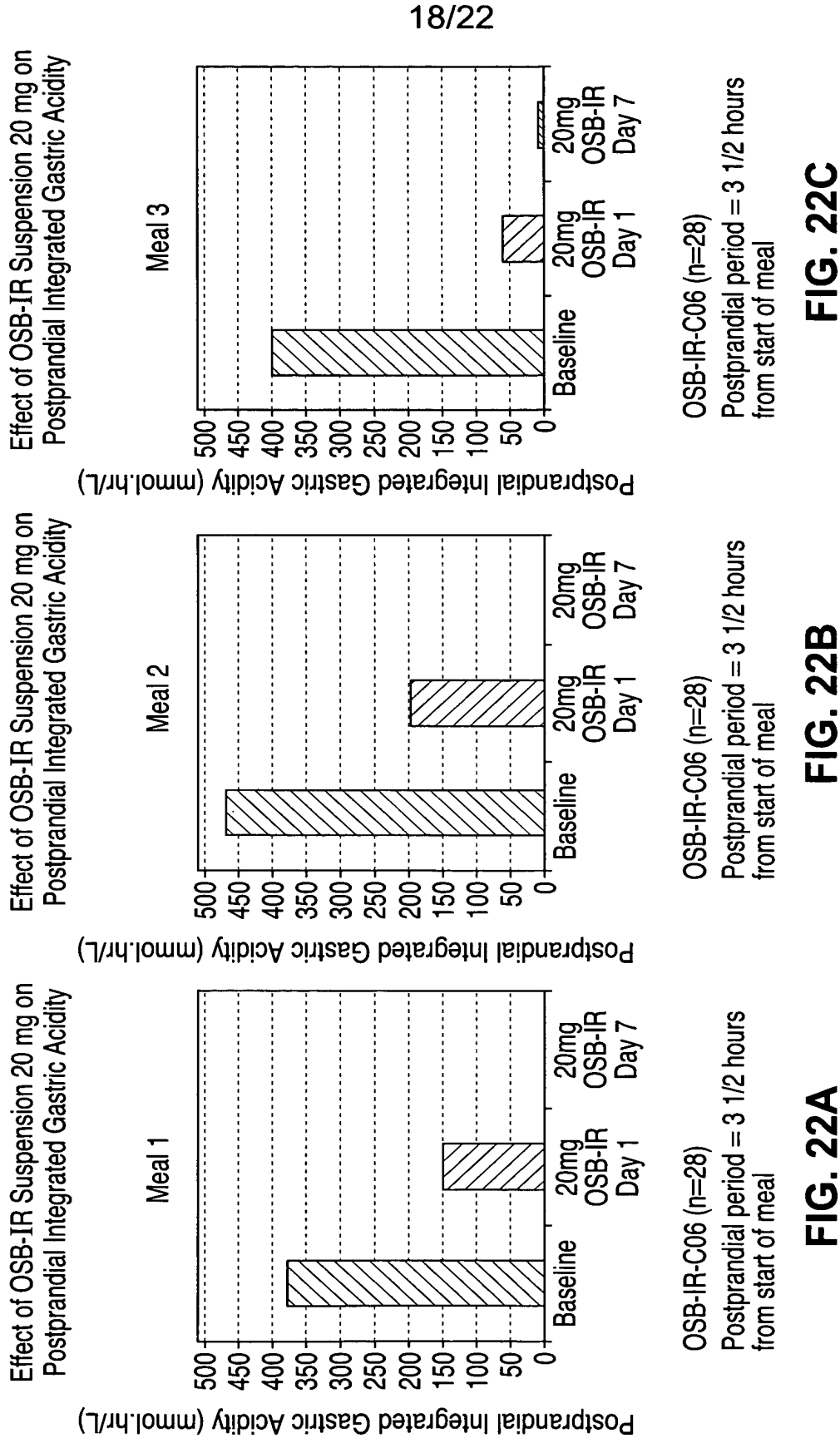
FIG. 21B

Median Gastric pH Over 24 Hours After Administration  
Of OSB-IR Suspension (Steady State)



% Time pH > 4  
Control 4% - 1 hr  
OSB-IR 20 mg Day 7 50% - 12 hrs  
OSB-IR-C06 (n=28)

FIG. 21A



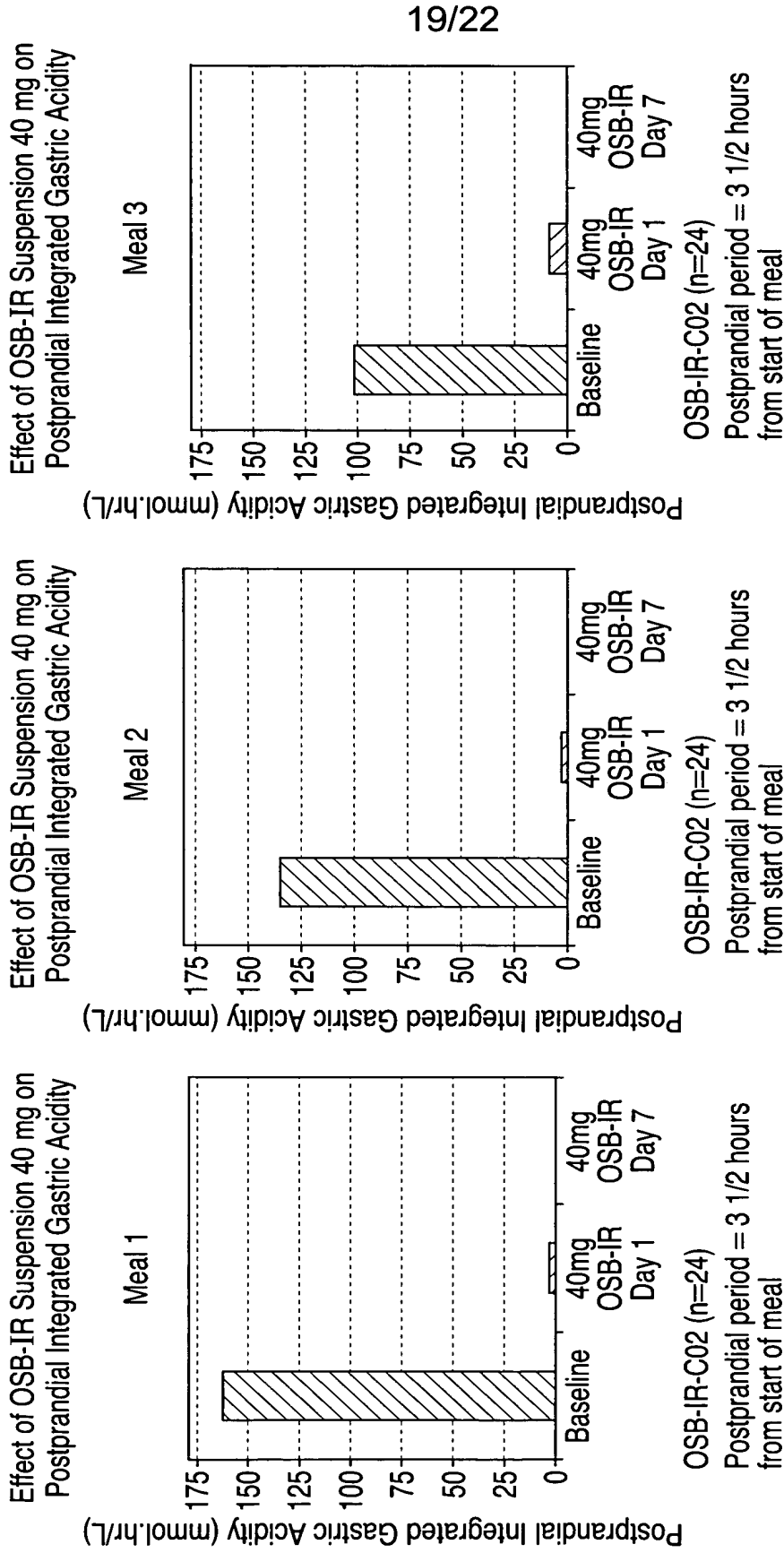


FIG. 23A

FIG. 23B

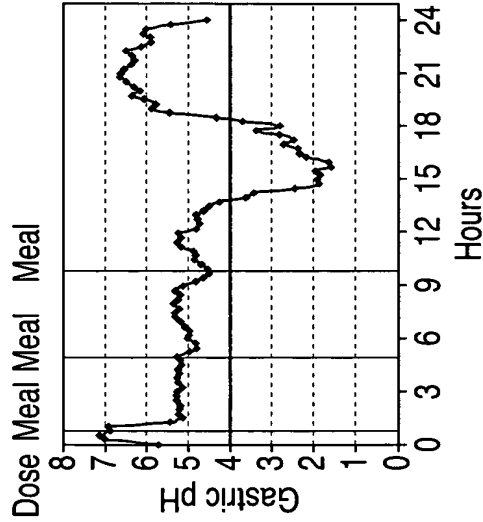
FIG. 23C

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Effect of Dosing Regimen on  
Median Gastric pH Over 24 Hours

40 mg qAM

Day 7



OSB-IR-C02

% Time pH > 4 78%

Note: Zero time is the 15-minute time interval prior to the time of dosing. Values are displayed for each 15-minute time interval of the 24-hour postdose recording period. Values are medians.

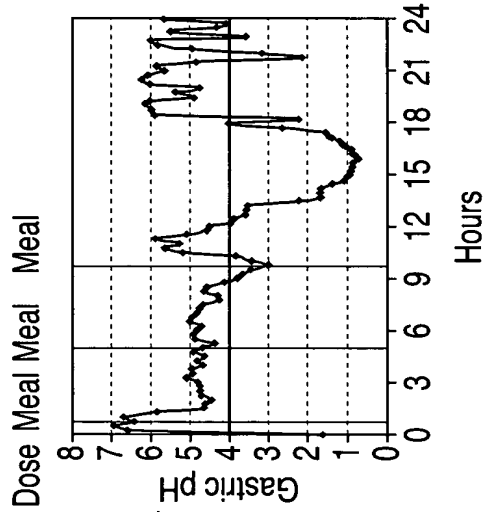
OSB-IR-C02 (n=24);  
OSB-IR-C06 (n=17)

**FIG. 24A**

Effect of Dosing Regimen on  
Median Gastric pH Over 24 Hours

20 mg qAM

Day 7



OSB-IR-C06

% Time pH > 4 56%

Note: Zero time is the 15-minute time interval prior to the time of dosing. Values are displayed for each 15-minute time interval of the 24-hour postdose recording period. Values are medians.

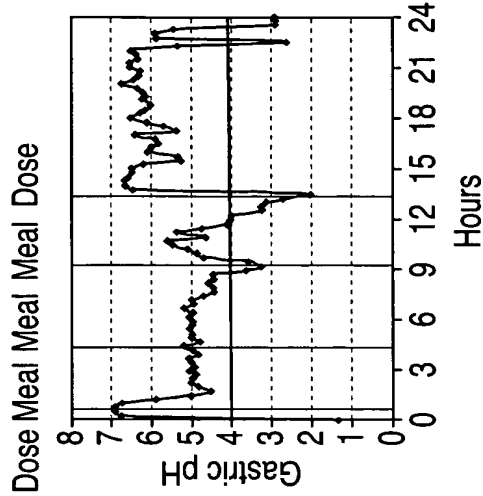
OSB-IR-C02 (n=24);  
OSB-IR-C06 (n=17)

**FIG. 24B**

Effect of Dosing Regimen on  
Median Gastric pH Over 24 Hours

20 mg b.i.d.

Day 8



OSB-IR-C06

% Time pH > 4 79%

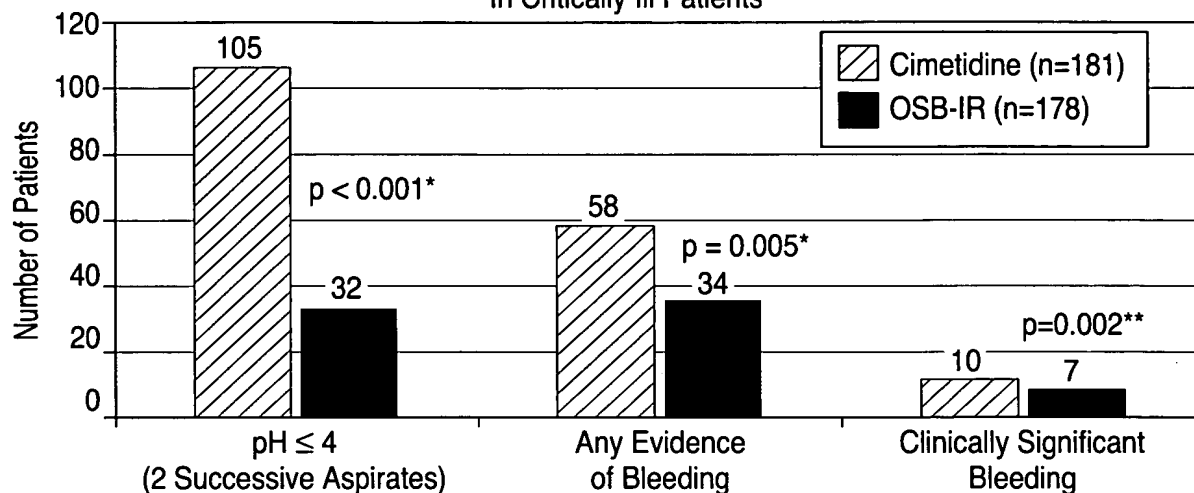
Note: Zero time is the 15-minute time interval prior to the time of dosing. Values are displayed for each 15-minute time interval of the 24-hour postdose recording period. Values are medians.

OSB-IR-C02 (n=24);  
OSB-IR-C06 (n=17)

**FIG. 24C**

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### pH Control and Upper GI Bleeding In Critically Ill Patients



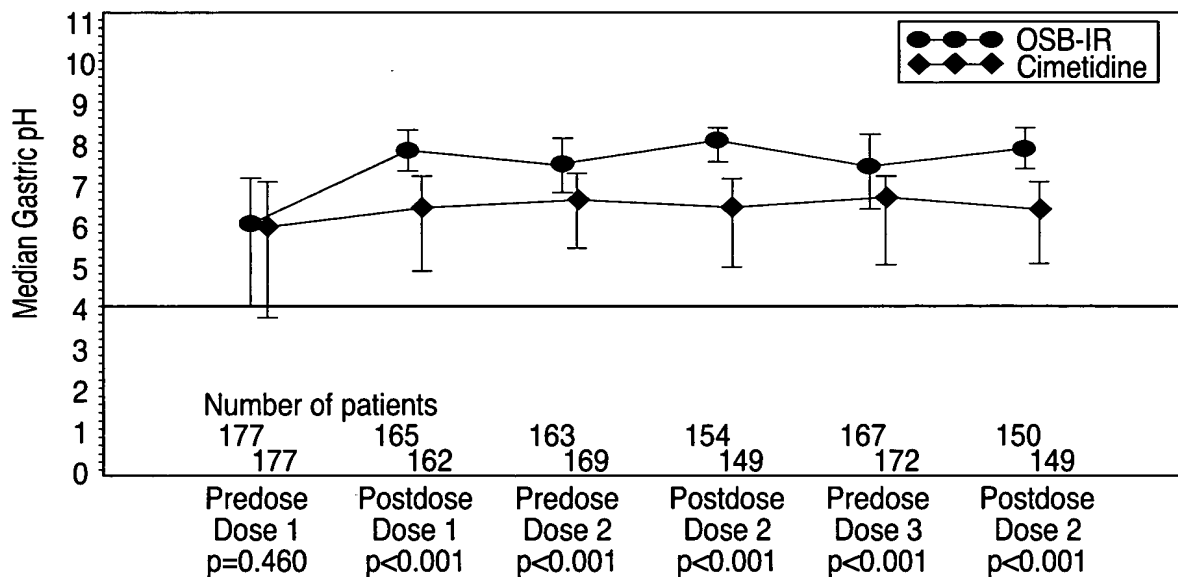
OSB-IR-C03 (n=359)

\* 2-sided Fisher's Exact test

\*\* 1-sided non-inferiority analysis

**FIG. 25**

### Median Gastric pH in Critically Ill Patients Dosed with OSB-IR Suspension 40 mg or IV Cimetidine (First Two Days of Dosing)



OSB-IR-C03 (n=359)

Predose samples obtained immediately before dosing; postdose samples obtained one hour after dosing.

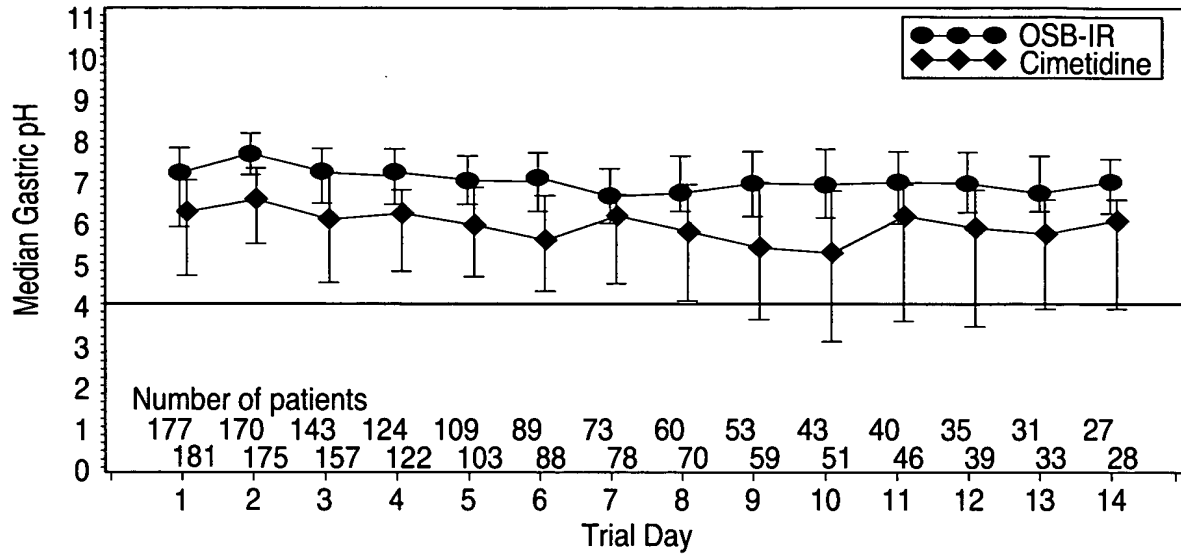
P-values were not adjusted for multiple comparisons.

The median gastric pH was calculated for each patient for each trial day. The median and the 25th and 75th percentiles of these by-patient medians are displayed here.

**FIG. 26**

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Median Gastric pH in Critically Ill Patients Dosed with OSB-IR  
Suspension 40 mg or IV Cimetidine

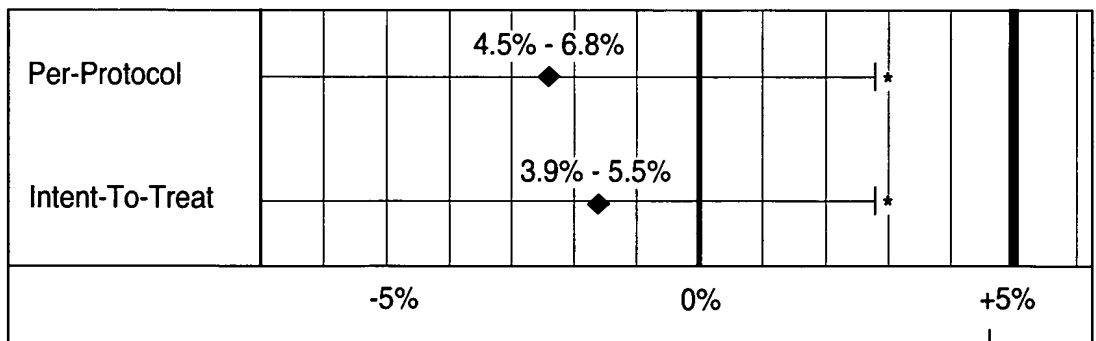


OSB-IR-C03 (n=359)

The median gastric pH was calculated for each patient for each trial day. The median and the 25th and 75th percentiles of these by-patient medians are displayed here.

**FIG. 27**

Non-inferiority Analysis for the Difference in Bleeding Rates  
(OSB-IR Bleeding Rate minus Cimetidine Bleeding Rate)



PP: n = 303, p = 0.003

ITT: n = 359, p = 0.002

\*Boundary of one-sided 97.5% confidence interval.

Non-inferiority Margin  
(protocol defined)

**FIG. 28**